REMARKS

Claim 83 was previously pending and was rejected. New claims 111-115 have been added. Support for the new claims can be found throughout the original application. Support for new claim 111 can be found throughout the original specification, and *inter alia*, at paragraph **[0085]**. Support for new claims 112, 114, and 115 can be found throughout the original specification, and *inter alia*, at pages 27-29 in paragraphs **[0127]** – **[0132]**. Support for new claim 113 can be found throughout the original specification, and *inter alia*, at paragraphs **[0232]** and **[0301]**. Support for new claims 114 and 115 can be found throughout the original specification, and *inter alia*, at paragraphs

Entry of the amendments and consideration on the merits is respectfully requested.

There is no rejection of the elected invention over the prior art.

With respect to all amended and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicant has carefully considered the points raised in the Office Action and believes that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Information Disclosure Statement

Applicants appreciate the Office's acknowledgement and consideration of the Information Disclosure Statement (IDS) filed on 21 December 2007.

Regarding the Canadian and EP office actions which were considered but crossed out as allegedly not being published documents and not conforming to the requirements discussed in 37 C.F.R. § 1.98, Applicants disagree that these documents are not proper references.

"An information disclosure statement filed in accordance with the provisions of 37 C.F.R. § 1.97 and 37 C.F.R. § 1.98 will be considered by the examiner assigned to the application." M.P.E.P. § 609. Information such as "patents, publications, applications, or other information" is properly submitted for consideration by the Patent Office. 37 C.F.R. § 1.97(a)(1), (emphasis added). A publication is a document that has been disseminated or publicly available to those of ordinarily skilled in art, such that it can be reasonably located, recognize, and comprehend. *In re Wyer,* 655 F.2d 221, 226 (CCPA 1981); M.P.E.P. § 2128.

The M.P.E.P. and the C.F.R. make clear that it is the Examiner's affirmative duty to consider any properly submitted reference. Office actions from countries where the prosecution file histories are available to the public meet the legal requirements of a publication and thus are properly considered as references.

In Canada "all patent applications, except those filed prior to October 1, 1989 and documents on file in connection therewith, shall be open to public inspection after the expiration of an eighteen-month confidentiality period (subsection 10(2) of the [Canadian] Patent Act)." MOPOP § 2.01.01, available at http://strategis.ic.gc.ca/sc_mrksv/cipo/patents/mopop/mopop-e.html, last viewed July 11, 2008 (emphasis added). Similarly, EP applications are published eighteen months after filing, after which time the application and the contents of the file history are available to the public. Article 128(4) of the EPC, available at http://www.epo.org/patents/law/legal-texts/html/epc/2000/e/ar128.html, last viewed July 11, 2008. The Office Actions for Canadian Application No. 2,440,147 and EP application No. 02 723 291.7 were thus available to the public at the time the documents were placed into the respective prosecution files. The Office Actions were part of the prosecution files at the time they were sent to Applicants' associates in Canada and Europe: August 2, 2007 and August 17, 2007, respectively. These are the dates listed on the first page of each reference. Accordingly, these documents are publications.

The Examiner is thus requested to consider the previously submitted documents or state on the record that it is the position of the Patent Office that such documents do not constitute prior art and that Applicants for patents are under no duty to disclose such documents.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claim 83 was rejected for lack of enablement. The Office maintained that the specification, while being enabling for an isolated 121P1F1 transcript that encode the protein of SEQ ID NO:2, does not reasonably provide enablement for any isolated transcript variants that encodes a protein comprising at least one amino acid substitution, addition or deletion relative to SEQ ID NO:2 or the transcript variant of SEQ ID NO:5. The Examiner is essentially asserting that there is no objective evidence that the transcript variant specified in the claim possess the same properties as the generic 121P1F1 sequence, such that the transcript variants are over-expressed in cancers. The Examiner stated that "Applicant has not taught how to make and use a transcript variant that encodes SEQ ID NO:5 because the instant application does not disclose the genus of transcript variants encoding SEQ ID NO:5 which share the function(s) and/or characteristic(s) of the 121P1F1 protein of SEQ ID NO:2, e.g., highly expressed in prostate cancer. The specification does not provide sufficient guidance as to which isolated 121P1F1-related protein (e.g., SEQ ID NO:5) would share the same function as the 121P1F1 protein of SEQ ID NO:2, if known. Neither does the specification provide any working examples of any 121P1F1-related protein (e.g., SEQ ID NO:5) that have the same functional activities or characteristics, i.e., highly expressed in prostate cancer as the 121P1F1 protein of SEQ ID NO:2." (OA at page 4).

Applicants disagree, and respectfully traverse the rejection.

For sake of clarification, please note that SEQ ID NO:2 as claimed in U.S. Patent No. No. 6,924,358 ("the '358 patent") and USSN 11/125,805 corresponds to SEQ ID NO:3 in the current application. SEQ ID NO:5 is a transcript variant of SEQ ID NO:3, and is thus expressed by the same gene. Amino acid residues 1-92 of SEQ ID NO:5 (a 126 a.a. residue polypeptide) are identical to amino acid residues 1-92 of SEQ ID NO:3, as shown in Figure 11. Moreover, as shown in Figure 10, nucleic acid residues 1-358 and 518-1028 of SEQ ID NO:4, which encodes SEQ ID NO:5, are identical to nucleic acid residues 1-867 of SEQ ID NO:2, which encodes SEQ ID NO:3. Therefore, every nucleic acid residue of SEQ ID NO:2 is also present in SEQ ID NO:4. Claim 1 has been amended to reflect the appropriate SEQ ID NO, and reflect that the encoded protein is immunoreactive with an antibody specific for amino acids 1-92 of SEQ ID NO:3.

The claims are narrowly drawn to specific polynucleotide and protein sequences can be prepared with a minimal quantity of experimentation. A working example discloses use of a claimed polynucleotide to detect a transcript that is highly expressed in cancer cells, but not highly expressed in normal cells. Therefore, one of skill in the art need not undertake undue experimentation to use the claimed polynucleotides. A consideration of the factors in *In re Wands* below shall show that undue experimentation is not required to practice the subject matter of claim 83.

Nature of the Invention. Claim 83 is narrowly drawn to a polynucleotide that encodes a protein having the sequence SEQ ID NO: 5, which protein is immunoreactive with an antibody that binds specifically to amino acids 1-92 of SEQ ID NO:3. The nature of the invention is such that undue experimentation is not required to prepare the polynucleotides or proteins of the above sequences since the sequences are extensively described.

Breadth of the Claims. The proteins encoded by the polynucleotides of the claimed subject matter encode for a protein having SEQ ID NO: 5 or the polynucleotides have at least a specific sequence, such as SEQ ID NO: 4. Since the claims are tailored to individual sequences, this factor weighs strongly in favor of enablement.

Quantity of Experimentation. There is a level of knowledge in the art such that the genetic code allows structure/function correlation between a polynucleotide and an amino acid sequence. Computer technology exists to allow one of skill in the art to apply the genetic code to arrive at a polynucleotide sequence within the scope of claim 83. Undue experimentation is not required to prepare a polynucleotide encoding a protein having a sequence of SEQ ID NO:5. No undue experimentation is required to prepare a polynucleotide containing the sequence of SEQ ID NO: 4.

One of ordinary skill in the art would reasonably conclude that an antibody to amino acids 1-92 of SEQ ID NO:3 would be capable of binding to the protein of SEQ ID NO:5 since the two share these 92 amino acids. Whether or not antibodies to this region also detect SEQ ID NO:5

could readily be determined using standard immunoassay technology which was notoriously well known in the art at the time the application was filed. Applicants acknowledge that screening every possible antibody would be time consuming and labor intensive, but such an effort would not rise to the level of undue experimentation.

Working Examples. The specification provides at least one working example involving the claimed polynucleotides, which are used in Northern Blot analysis of normal tissues and cancerous tissues. One of skill in the art can use this example to devise other assays relating to cancer using other polynucleotide sequences of the claimed subject matter.

The gene 121P1F1 was shown to be overexpressed in certain types of cancers (see Table 1) and page 5, lines 7-14. Applicants have asserted in the application that the claimed sequences have utility as diagnostic agents to identify prostate, bladder, kidney, colon, lung, pancreas, breast, cervix, and stomach cancer. Specification, page 5, paragraph **[0027]**, page 96, paragraph **[0373]**; Table I; and Figures 20 and 21. (All citations to the specification are based upon the substitute specification submitted April 4, 2007). The present application contains evidence that the novel gene which encodes the target protein expresses mRNA in cancer. "121P1F1 expression was seen in kidney, breast, cervix, and stomach cancers. 121P1F1 was also found to be highly expressed in a panel of cancer cell lines." Specification, page 11-12, paragraph **[0052]**; see also Figure 21. "121P1F1 expression was also shown in prostate cancer xenografts and in all cancer cell lines tested, such as in prostate . . . ; bladder . . . , kidney . . . ; colon . . . and in the cancer cell lines 293T, FE-Es and KCL.22". Specification, page 96, paragraph **[0093]**; see also Figures 17-19. The specification also shows that the target gene is expressed in normal testis and in thymus and ovary, but not in normal prostate. See Figure 18. 121P1F1 mRNA was detected by RT-PCR and Northern blotting. As described above and shown in Figure 10, nucleic acid residues 1-867 of SEQ ID NO:2 are *identical* to nucleic acid residues 1-358 and 518-1028 of SEQ ID NO:4, which encodes SEQ ID NO:5. Thus, detection of SEQ ID NO:2 by RT-PCR and Northern blotting also detects SEQ ID NO:4, which encodes SEQ ID NO:5.

Furthermore, the polynucleotide sequence encoding SEQ ID NO:5 is a naturally-occurring transcript variant of the nucleotide sequence comprising SEQ ID NO:1 that encodes SEQ ID NO:2. The specification provides ample disclosure with regard to expressing a 121P1F1 polypeptide in a host cell. For instance, Example 6, entitled "Production of Recombinant 121P1F1 in Prokaryotic Systems," discloses protein expression in prokaryotic host cells and describes a number of expression vectors which may be employed therefor. Similarly, Example 7 and Figure 14 teach production of recombinant 121P1F1 in eukaryotic expression systems. Applicants also fully describe methods for ge nerating polyclonal and monoclonal antibodies to 121P1F1. For example, Example 9, entitled "Generation of 121P1F1 Polyclonal Antibodies," discloses the generation of antibodies to 121P1F1 polypeptides or immunogenic portions thereof. The specification notably discloses the generation of a polyclonal antibody to the full-length 121P1F1 polypeptide. Figures 13 and 14 show that the "polyclonal antibody shows strong reactivity to MYC-HIS tagged 121P1F1 in transfected T cells and also to several proteins in the tumor cell lines, indicating reactivity to endogenous 121P1F1 and to variant molecules of different molecular weights." Specification, pages 111-112, paragraph **[0427]**; see also Figures 13 and 14. Figure 13 shows that the polyclonal antibody to 121P1F1 showed strong reactivity to variants of 121P1F1 in a number of cancer cell lines, including bone, bladder, lung, colon, and pancreatic cancer cell lines. Applicants have thus amply demonstrated that variants of 121P1F1 are expressed in cancer cells despite the differences in the amino acid sequences of the variants, and that those antibodies to 121P1F1 and/or its variants are thus useful as diagnostics. Again, it is noteworthy that claim 83 has been to recite that the claimed variant is immunoreactive with an antibody that binds to amino acids 1-92 of SEQ ID NO:3, which is identical to the sequence in the claimed sequence.

This is not a situation where the splice variant is unknown: the claimed sequence of the variant is disclosed as SEQ ID NO:5. The splice variant was identified by the use of EST data in an EST assembly approach. Specification, Example 5, page 99, paragraph **[0385]**. The specification further provides that the parameters of a splice variant can be confirmed using "a variety of techniques are available in the art, such as full-length cloning, proteomic validation, PCR-based validation, and 5' RACE validation, etc." Specification, page 99, paragraph **[0383]** (citations omitted). It is further known that genomic regions are modulated in cancers. When the genomic

region to which 121P1F1 maps is modulated in a particular cancer, the splice variants of 121P1F1 are modulated as well. The specification thus provides that splice variants of 121P1F1 that are structurally and/or functionally similar to 121P1F1 – which was shown in the specification to have a particular expression profile – will share this expression pattern, and thus the splice variants can serve as tumor-associated markers/antigens. All of this data, taken as a whole, is more than sufficient to demonstrate that it is more likely than not to one of ordinary skill in the relevant art that the presently claimed invention is useful for the detection of cancers.

Guidance in the specification. One of skill in the art is also provided sufficient guidance in the specification on how to conduct tests related to detection of cancer markers using the claimed polynucleotides.

State of the prior art and predictability in the art. It is predictable that using probes to detect SEQ ID NO:2 would also detect the polynucleotide of SEQ ID NO:4 since every nucleic acid residue of SEQ ID NO:2 is also present in SEQ ID NO:4. It is also predictable that an antibody specific to amino acids 1-92 of SEQ ID NO:3 would bind to and detect SEQ ID NO:5.

Level of skill in the art. The level of skill in the art is high.

Conclusion: The claims narrowly drawn to specific polynucleotide and protein sequences can be prepared with a minimal quantity of experimentation. A working example discloses use of a claimed polynucleotide to detect a transcript that is highly expressed in cancer cells, but not highly expressed in normal cells. Applicants have shown that antibodies to SEQ ID NO:3 specifically detect the protein at high levels in cancerous tissues. Thus, antibodies that detect amino acids 1-92 of SEQ ID NO:3 are also useful for detecting SEQ ID NO:5, which shares this region of identity. Therefore, one of skill in the art need not undertake undue experimentation to use the claimed polypeptides and polynucleotides.

Therefore, Applicants respectfully submit that the specification satisfies the enablement requirement of 35 U.S.C. § 112, First Paragraph, with respect to claim 83. Accordingly, it is believed this basis for rejection may be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 83 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner asserted that the recitation "which variant is immunoreactive with at least one antibody that specifically binds the amino acid sequence of SEQ ID NO:2" was unclear since it was not apparent whether the transcript variant of SEQ ID NO:1 was immunoreactive with an antibody that binds the amino acid sequence of SEQ ID NO:2 or if the protein of SEQ ID NO:5 is immunoreactive with an antibody that binds the amino acid sequence of SEQ ID NO:2. The amendments to claim 83 obviate the rejection and make it clear that the protein of SEQ ID NO:5 is immunoreactive with an antibody that binds amino acids 1-92 of SEQ ID NO:3. Accordingly, it is believed this basis for rejection may be withdrawn.

CONCLUSIONS

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 511582003420. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: July 14, 2008

Respectfully submitted,

By: /Elizabeth Cary Miller/
Elizabeth Cary Miller
Registration No.: 54,708
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 314-7717